

TB ISSUES AND UPDATES

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WV Infectious Disease Symposium
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Health Departments in West Virginia



Dr. Fauci's Opinion Concerning TB

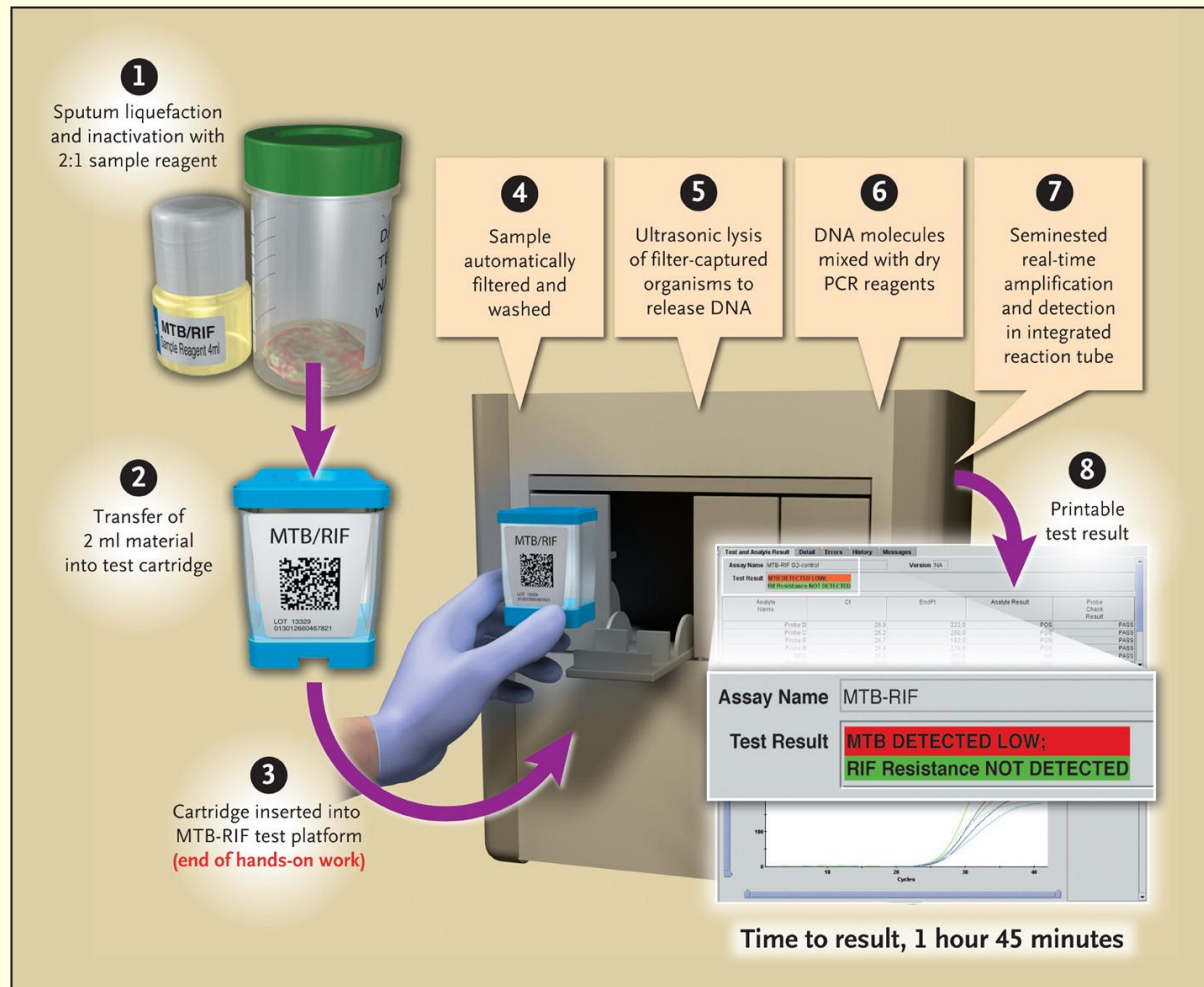
“The consequences of inattention to TB research are not just embarrassing, they are tragic and shameful. Generations of research advances and technologies have bypassed the field of TB research. All of the great breakthroughs that we have seen in molecular biology – there was nobody working on it in TB. Nine million people develop active TB each year and yet we still don’t have an effective vaccine. There have been no newly licensed drugs for TB in forty years (with the exception of Rifabutin). The therapeutic regimens, although they work, are cumbersome and prone to the development of drug resistance. The diagnostics are ridiculous, they are antiquated, non-standardised and imprecise.”

Tony Fauci, M.D., Director

U.S. National Institute of Allergy and Infectious Diseases (NIAID)

Cape Town – IAS 2009

GeneXpert



GeneXpert (Nucleic Amplification Test)

Rapid diagnosis of TB especially if sputum is smear positive

Rapid determination of multiple drug resistant TB organisms

Greatly reduces need for contact investigation

Reduces unnecessary treatment with potentially toxic drugs

Study of 156 patients in San Francisco, CA with GeneXpert guided treatment reduced over-treatment by 94% without reducing early detection of TB patients.

- J.Lucien Davis et al. American Journal of Respiratory and Critical Care, 2014

All tests, so far, are producing great results compared to TB cultures. The GeneXpert procedure is much simpler than the TB cultures and results are produced much faster.

Interferon Gamma Release Assays (IGRAS)

- **Blood test more specific than TB skin test in certain populations**
- **Requires only one visit for testing**
- **Objective interpretation**

- **Excellent for assessing latent TB infection (LTBI) in the foreign-born with prior Bacille Calmette Guerin (BCG) immunization**
- **Better accepted by patients as being specific for tuberculosis**
- **Reduces overtreatment for LTBI**
- **Very useful in suspect false positive skin test**
- **Occasionally falsely positive when screening large groups of low-risk individuals**

- **Persons who are foreign born**
- **Persons who have had BCG vaccine**
- **Persons who are HIV infected**
- **Persons who are a known or suspect contact to an active case of TB believed to be at risk for follow-up to tuberculin skin test (TST) reading**
- **Persons with positive purified protein derivative (PPD) without any known risk factors as ordered by TB clinician**

Comparison of Gamma Interferon and Tuberculin Skin Test

Interferon-Gold-Release Assay performed better than tuberculin skin test in predicting who in control group of those household contacts which refused prophylaxis would develop active tuberculosis.

Diel, R. et al. – AMJ Resp. Crit. Care Med 2011 Jan 1; 183:88. German study of contacts of Active tuberculosis cases

T-Spot outperformed tuberculin skin test in predicting which silicotic subjects that refused prophylaxis would develop tuberculosis.

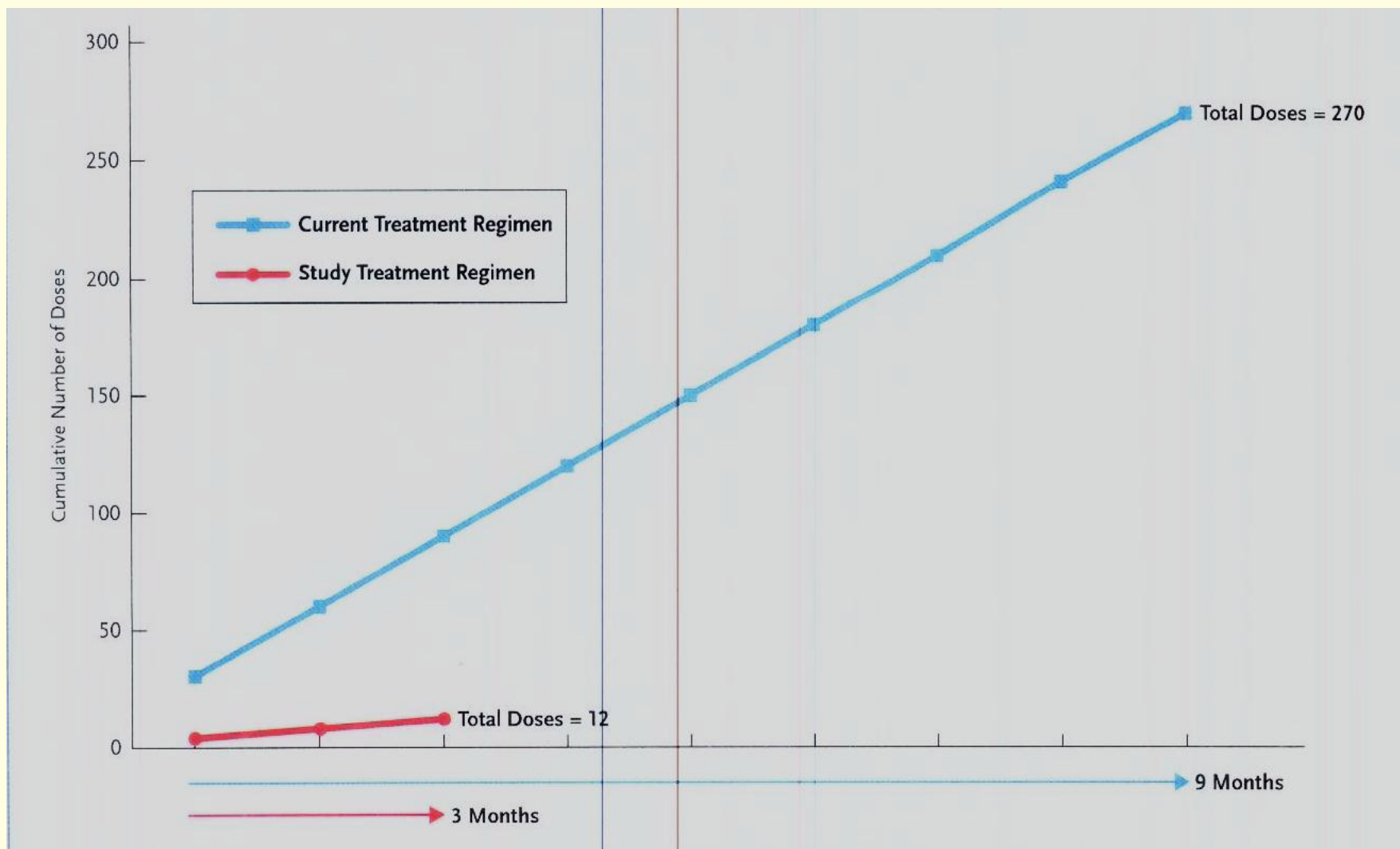
Leung, C. C. et. al. – AMJ Resp. Crit. Care Med 2010; 182:834-840

Prophylaxis for LTBI

- **Isoniazid (INH) daily for 9 months
(self-administered)**
- **Rifampin daily for 4 months
(self-administered)**
- **Isoniazid and Rifapentine once weekly for 12
weeks (Directly Observed Therapy)**

Treatment of Latent TB Infection

Cumulative Doses Required, Current vs. Study Regimen



Rifapentine/INH Treatment

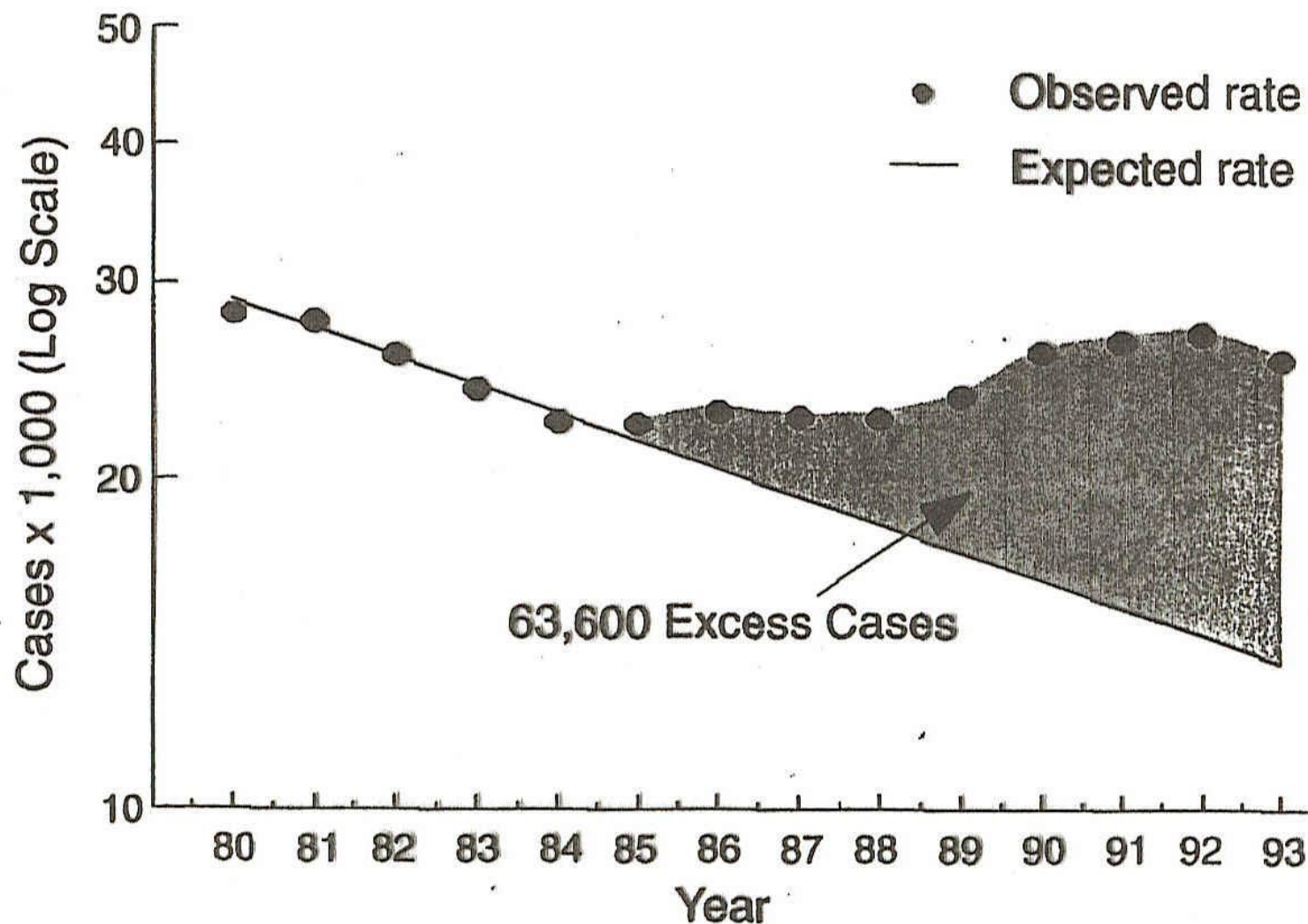
- **Less hepatotoxicity – 0.4% vs 1-2% with INH**
- **Substantial improvement of prophylaxis completion (75% vs 53% with INH)**
- **Cost is favorable to other options**
- **Occasional intolerance requiring hydration**

Little Old Ladies Tell Lies (Directly Observed Therapy)



Expected and Observed TB Cases

United States, 1980-1993



Increase in TB Mortality: 1985-1992

Factors include:

- Deterioration of the TB public health infrastructure
- HIV/AIDS epidemic
- Immigration from countries where TB is common
- Transmission of TB in congregate settings

The Patient May Not Take All the Drugs Prescribed

Factors:

- **Lack of resources**
- **Intolerance/toxicity**
- **Misunderstanding**
- **Interrupted drug supply**
- **Disbelief of the diagnosis**
- **Disbelief of the efficacy or necessity of the treatment**
- **Chaotic lifestyle; substance abuse**
- **Cultural issues**
- **Pregnancy**
- **Neuropsychiatric disease**
- **Absence of resolute Directly Observed Therapy (DOT) program**

Directly Observed Therapy (DOT)

- **Nonadherence is a major problem in TB control.**
- **DOT should be used with all regimens.**
- **DOT can lead to significant reductions in relapse and acquired drug resistance.**

MDR - TB

RATES OF MDR-TB AMONG PREVIOUSLY TREATED CASES OF TB IN SELECTED COUNTRIES/REGIONS

Country/Region	Year	% of MDR among PREVIOUSLY TREATED CASES	% of any resistance (1 or more drugs) among PREVIOUSLY TREATED CASES
Kazakhstan	2001	56.4	82.1
Lithuania	2002	53.3	67.9
Estonia	2000	45.3	58.1
Russian Fed. – Tomsk Oblast	2002	43.6	60.7
Russian Fed. – Orel Oblast	2002	42.4	73.3
Uzbekistan – Karakalpakstan	2001	40.2	79.4
Egypt	2002	38.2	68.2
China – Henan	2001	36.6	60.8
Latvia	2000	27.1	38.1
Ecuador	2002	24.8	47.4
Mexico (Baja CA, Oaxaca, Sinaloa)	1997	22.4	41.1
United States	2001	5.2	18.8

Source: WHO

For statistics from all geographic regions surveyed by WHO, see http://www.who.int/gtb/publications/drugresistance/2004/drs_report_1.pdf

TB Drug Resistance in WV

<u>YEAR</u>	<u>MONO</u>	<u>MDR</u>	<u>2 OTHER</u>
2013	4	0	0
2012	2	0	0
2011	1	0	0
2010	1	0	1
2009	3	0	0
2008	0	0	0
2007	1	0	1
2006	2	0	0
2005	3	0	0
2004	3	0	0
2003	0	0	1
2002	2	0	1
2001	5	0	0
2000	4	0	2
1999	2	0	2
1998	3	0	0
1997	3	0	0
1996	3	0	0
1995	1	0	1

The XDR-TB afflicted, the modern leper of biblical description, is the consequence of inadequate and incomplete tuberculosis treatment.

WV TB Elimination Objectives

1. Treat active TB
2. Prevent new cases of TB
3. Eliminate TB in WV

TB Incidence Rates by Year of Report

West Virginia and United States Decennial Rates, 1940-2000

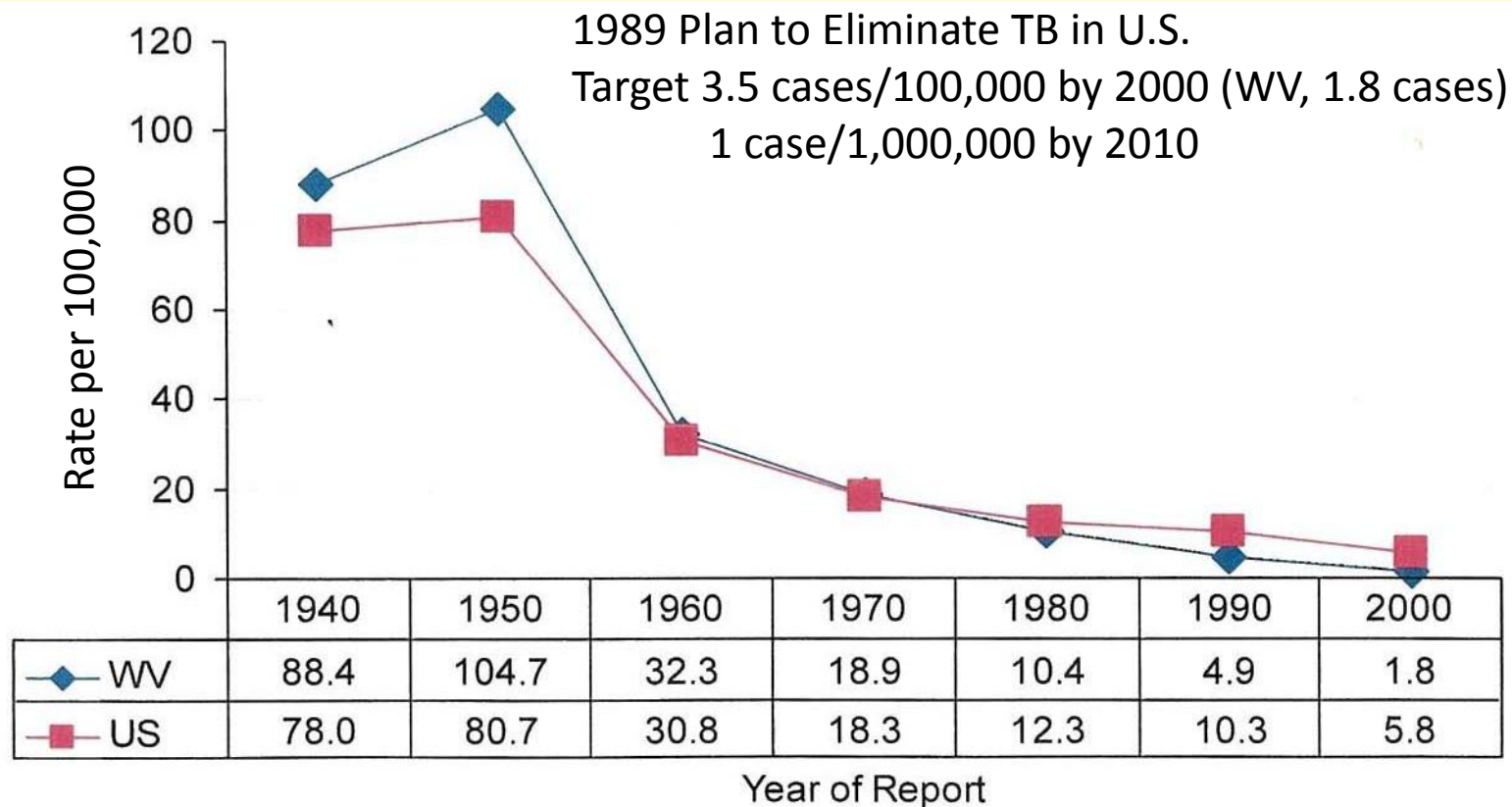


Figure 2

Data from West Virginia Tuberculosis Profile, 2005

- **Only disease for which the State of WV is committed to pay for treatment**
- **Only disease for which patient required to take treatment**

TB Programmatic Budget

	<u>2013</u>	<u>2014</u>	<u>2015</u>
<u>Federal</u>	\$148,960	\$49,053	\$28,383
<u>State</u>	\$246,175	\$103,298	\$99,417
<u>State (Gen. Rev)</u>	<u>\$29,512</u>	<u>\$49,480</u>	<u>\$49,512</u>
TOTAL	\$424,647	\$201,841	\$177,312

Budget does not include personnel & associated expenditures, i.e. fringe, etc.

Expenditures for TB Elimination

- Teach/Update County Health Nurses
- Treat Active TB
- Contact Investigation of Active Case
- Treat Latent TB in Contacts
- Evaluate High-Risk Groups
- Treat Latent TB in High-Risk Groups
- Clinic Referrals for Special Conditions
- Supplies for Legislative Mandates

Costs

1. DOT	\$30,000
2. IGRAS	\$130,000
3. Other Labs	\$20,000
4. Meds (incl. PPD)	\$80,000
5. Other	\$65,000

(vehicle, rent, CXRs & supplies, travel, clinicians, etc.)

Amount to sustain TB Division

At Status Quo \$335,000

Clinicians, CXRs & supplies, vehicle, rent, travel, etc.

Expenditures for TB Elimination

Activity

Cost

Teach/Update County Health Nurses
Conference

Cohort Review

\$10,000

Treat Active TB

1. Meds

\$20,000

2. Labs – Liver Function

\$5,000

3. X-Rays

\$10,000

Expenditures for TB Elimination

Activity (cont.)

Cost (cont.)

Contact Investigation of Active Case

1. Skin Testing	\$20,000
2. X-rays	\$20,000

Treat Latent TB in Contacts

1. Meds	\$5,000
2. Lab	\$5,000
3. DOT	\$5,000

Expenditures for TB Elimination

Activity (cont.)

Cost (cont.)

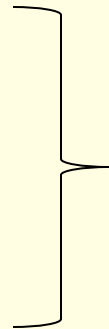
Evaluate High-Risk Groups

Hardy

Raleigh

WVU

Others



\$80,000

Treat Latent TB in High-Risk Groups

Meds

Lab

DOT

\$20,000

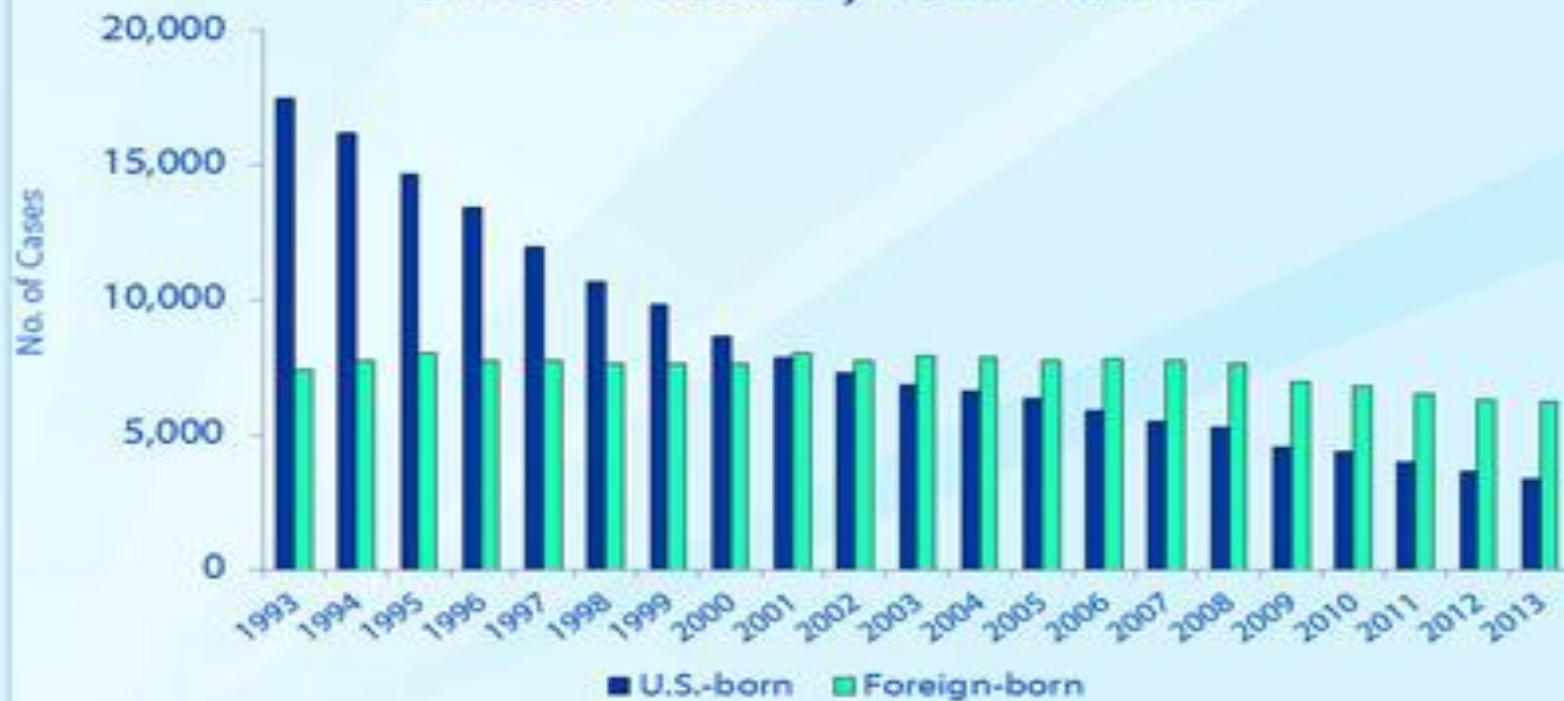
\$10,000

\$5,000

\$35,000

Foreign-Born TB Patients

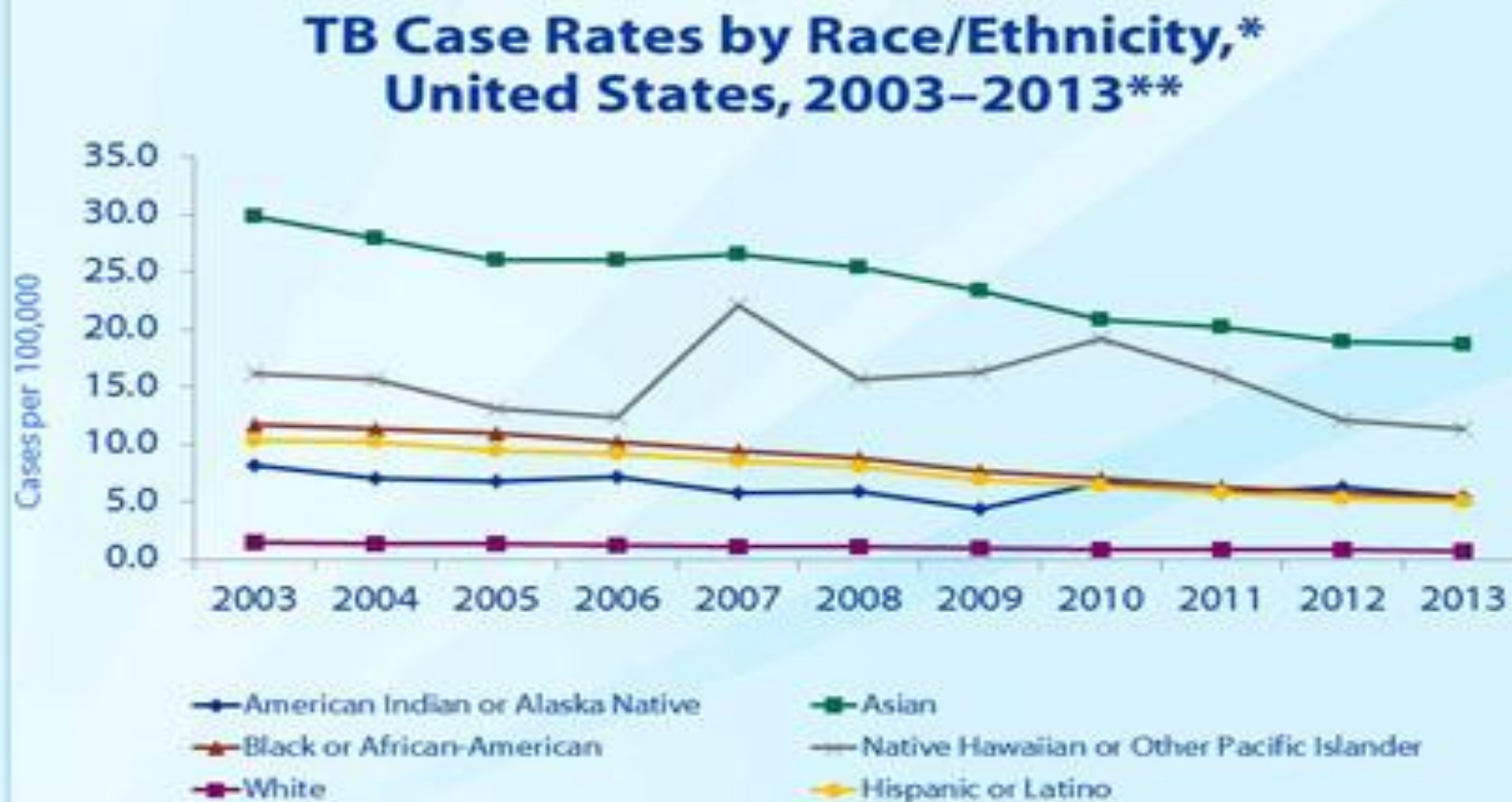
**Number of TB Cases in
U.S.-born vs. Foreign-born Persons,
United States, 1993–2013***



*Updated as of June 11, 2014.



Foreign-Born TB Patients



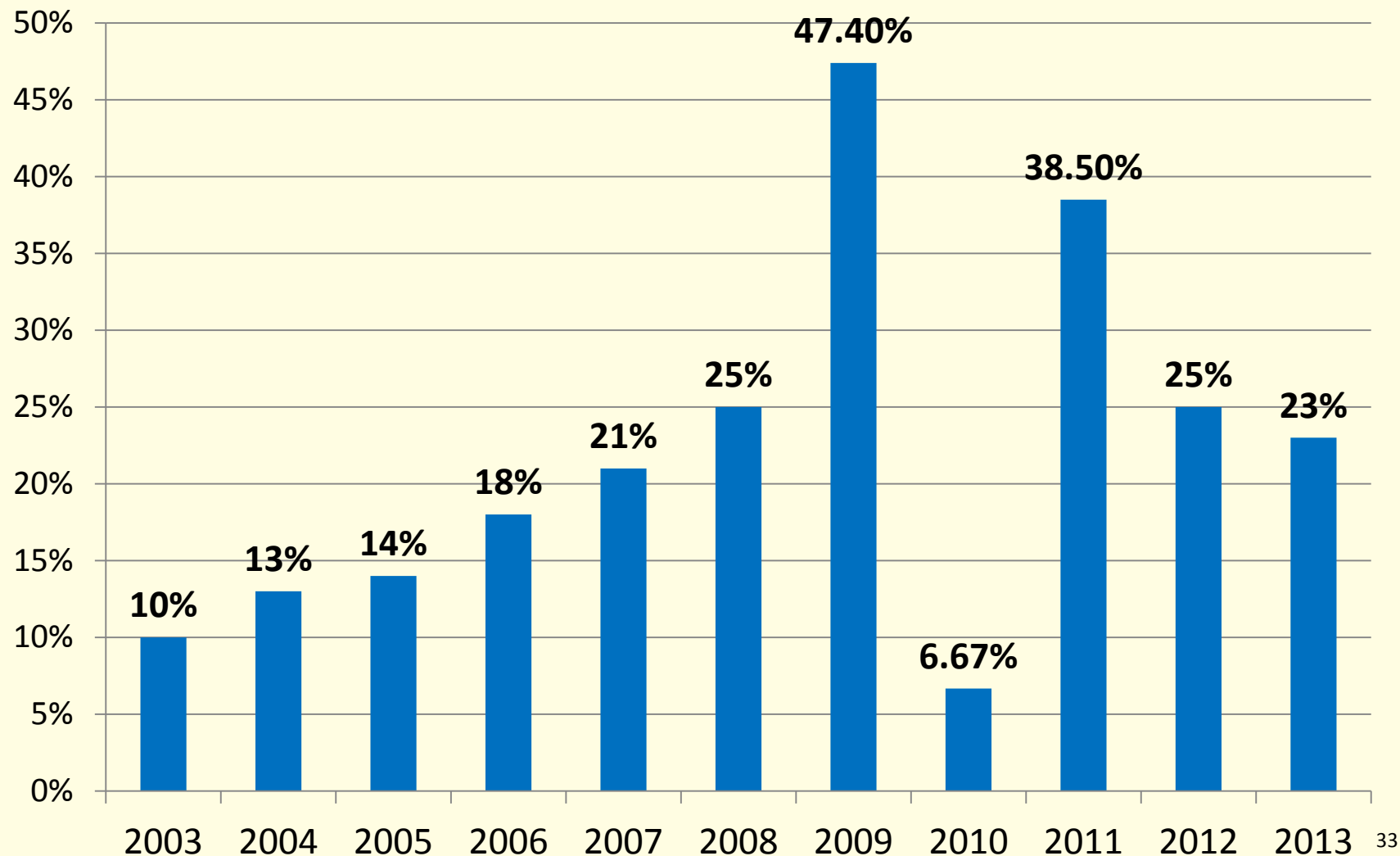
*All races are non-Hispanic.

**Updated as of June 11, 2014.



Foreign-Born TB Patients

Percentage of Foreign-Born TB Patients in WV, 2003-2013

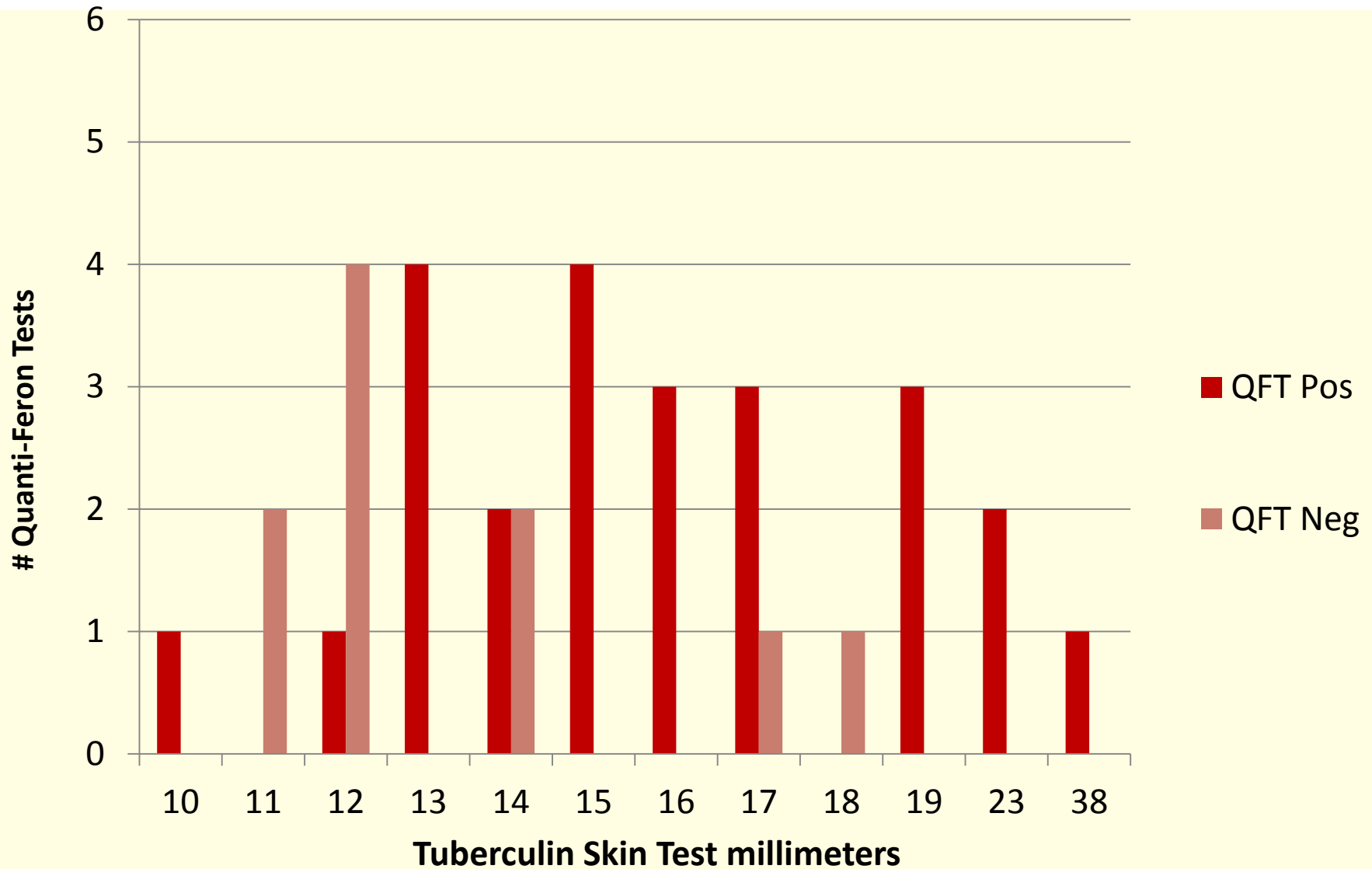


Revisiting Rates of Reactivation Tuberculosis

- **American Indian/Eskimo x 5**
- **Hispanic x 7**
- **African-American x 8**
- **Asian x 25**

MMWR, March 25, 2011. Incidence of TB in Ethnic Groups in the U.S. in 2010

IGRA vs. TST



Positivity Rate of Latent TB, 2013

School Personnel	0.22%
Contacts of TB Case	2.27%
Foreign-Born	8.00%
Homeless	2.38%
Hardy Co. Foreign-Born (82/339)	24.00%

Hardy County

1. How many foreign-born were assessed in the past 3 years? **339**
2. Which countries were they from? **Ethiopia, Haiti, Peru, Mexico, Nepal, Sudan, Ecuador, Burma/Myanmar, Eritrea, Bhutan, El Salvador, Philippines, and others.**
3. How many and what percentage were positive for latent TB? **(82) 24%**
4. What percentage of those with latent TB completed therapy?
5. Why is IGRAS the preferred form of assessment in this population?
6. How many active cases of TB have been prevented in this immigrant group?
5 - 8
7. How many secondary cases of TB have been prevented? **???**
8. Is this population less reluctant to take prophylaxis when confirmed by IGRAS?

Expenditures for TB Elimination

Activity (cont.)

Cost (cont.)

Clinic Referrals for Special Conditions

(Incidental positives in low-risk groups, immunosuppressed, homeless, drug dependency, routine immigration)

Clinician & X-Ray

\$20,000

T-Spot

\$20,000

TST

\$10,000

\$50,000

Supplies for Legislative Mandates

School Employees

Students

\$50,000

TOTAL

\$335,000

- 1. How many low-risk cases were referred to you last month because of positive skin test?**
- 2. What percentage of these had positive IGRAS?**
- 3. Why do low-risk infected persons have false positive PPDs?**
- 4. What would have been the approach to these persons without IGRAS?**
- 5. What's wrong with this approach?**

What to do?

What to do?

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